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Impact of Enhanced Recovery After Surgery Protocol Compliance on Outcome After Pancreatic Surgery

Results From a Certified ERAS Center

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Objective: The aim was to evaluate the sustainability of the pancreatic Enhanced Recovery After Surgery (ERAS) program and the effect of ERAS items on patient morbidity and hospital stay.

Background: The current ERAS guideline recommendations encompass 27 items to improve recovery after pancreatoduodenectomy (PD).

Methods: Patients who underwent pancreatic resection at the University Hospital Hamburg-Eppendorf between February 2016 and June 2023 were included. The datasets were retrospectively collected from a central database. The effects of individual ERAS items and compliance on morbidity and hospital stay were assessed by uni- and multivariable analyses.

Results: In total, 594 patients who underwent PD (44.8%), distal pancreatectomy (14.6%), total pancreatectomy (17.8%), or other pancreatic resections (22.7%) were included. Of these, 90 patients (15.2%) achieved a high overall ERAS compliance of ≥70%. High compliance was associated with significantly less complications (Clavien–Dindo ≥ 3a), reduced 30-day mortality, and a shorter hospital stay. Early mobilization on the first postoperative day (POD1), restrictive intravenous fluid administration, and timely removal of urinary catheters were significant multivariable predictors for lower morbidity. Early mobilization on POD1 also correlated with reduced morbidity in the subcohort of PD cases.

Conclusions: The pancreatic ERAS protocol can be sustainably implemented and applied to both, PD and non-PD cases. A high level of compliance with the ERAS protocol after pancreatic resections correlated with improved outcomes but was achieved by less than one-fifth of patients. Early mobilization on POD1 and restrictive fluid management were key indicators for optimized short-term outcomes.

Keywords: compliance, enhanced recovery after surgery, pancreatic surgery

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INTRODUCTION

Enhanced recovery after surgery (ERAS) protocols are used in an aim to implement evidence-based perioperative interdisciplinary standards and minimize surgical stress.[1,2] As in other fields of gastrointestinal surgery (eg, colorectal surgery), meta-analyses of the available reports have demonstrated that the implementation of ERAS can also reduce postoperative complications and shorten the length of hospital stay following pancreatoduodenectomy (PD).[3,4] The first guideline recommendations for pancreatic surgery were published >10 years ago and currently include 27 updated items.[5] The implementation of ERAS in pancreatic centers in the early phase is challenging, and a professional setup that includes a multidisciplinary motivated team has become necessary to achieve high ERAS compliance.[6] However, not all ERAS item recommendations are based on high-level evidence and need to be continuously challenged. In line with this, the current scientific literature lacks answers to whether an established pancreatic ERAS setting is effective and which ERAS items have the most significant impact on postoperative outcomes in the long term.

Therefore, the aim of the present study was to examine the correlation between single ERAS items and overall compliance with postoperative morbidity and hospital stay duration over an 8-year period at an ERAS-certified pancreatic center of excellence.

METHODS

Enhanced Recovery After Surgery Program and Patient Selection

All patients enrolled in the ERAS program at the University Hospital Hamburg-Eppendorf who underwent pancreatic surgery between February 2016 and June 2023 were retrospectively analyzed from a prospectively maintained database (ERAS Interactive Audit System [EIAS], www.erassociety.org, ENCARE, Krista, Sweden). Data were extracted in June 2023. The cohort study was conducted at the single academic ERAS Center of Excellence with a multidisciplinary ERAS team. ERAS was fully implemented in February 2016 at our institution. The local ERAS pathway is described in Supplemental Table 1, see http://links.lww.com/AOSO/A414. ERAS was applied for all pancreatic resections, including PD, distal pancreatectomy (DP), total pancreatectomy (TP), duodenum-preserving pancreatic head resection (DPPHR), enucleation, and pancreas segment resection. A multivisceral resection was defined as atypical or anatomical resection of an additional organ except pancreas, duodenum, gallbladder, or spleen in case of DP or TP. Atypical liver resections were included as well. Follow-up was conducted 30 days after the primary surgery. The internal standard was that patients were only registered in the EIAS if preoperative counseling was completed. All patients were older than 18 years and provided informed written consent. To compare ERAS outcomes over time, the study inclusion period was split into 3 periods: 2016 to 2018, 2019 to 2020 and 2021 to 2023. Notably, the ERAS program was paused in October 2020 because of the COVID-19 pandemic, and no patient data from that month were included. The study was approved by the local ethics committee (PV3548-1992-BO-ff). The Strengthening the Reporting of Observational Studies in Epidemiology guidelines and Reporting on ERAS compliance, outcomes and elements research checklists were followed.[7,8]

Definition of Outcomes

Compliance was defined as the fulfillment of individual pre-, intra-, and postoperative ERAS elements and was documented as compliant, noncompliant, or missing.[5] The calculation of compliance was performed before the update (EIAS version 5.7.9) of the EIAS was made in September 2023. Total compliance was calculated as the sum of individual compliance with the ERAS intervention relative to all recommended ERAS items. A compliance ≥70% was considered high.[6,9] The compliance definitions for the individual ERAS items are summarized in Supplemental Table 2, see http://links.lww.com/AOSO/A414.

The length of hospital stay was based on the day of admittance and the day of discharge. If readmission occurred within 30 days postoperatively, the duration of the secondary stay was added to the primary stay.

Complications were defined as any adverse event within 30 days after the primary operation and were graded according to the Clavien–Dindo classification (CDC).[10] A grading of CDC ≥ 3a was considered a major complication. For pancreatic surgery-specific complications, including postoperative pancreatic fistula (POPF), delayed gastric emptying (DGE), and post-pancreatectomy hemorrhage, published classifications of the International Study Group of Pancreatic Surgery were used.[11–13] The mobilization goals on postoperative days (PODs) 1, 2, and 3 were >2, >6, and >6 hours, respectively, throughout the study period according to initial ERAS recommendations[14]

Patients' general performance was classified according to the American Society of Anesthesiologists score and World Health Organization performance score.[15,16] The malnutrition status was assessed based on body mass index and the Nutritional Risk Score 2002.[17]

Statistics

Unless otherwise indicated, values are shown as absolute numbers and percentages, and quantitative variables are shown as medians and interquartile ranges (IQRs). Group differences were evaluated by the Mann–Whitney *U* test, 2-tailed Student *t* test, or analysis of variance, as applicable. Categorical variables were compared with Fisher exact or the χ^2 test for univariable analysis. Missing data were not defaulted to negative. Multivariable analysis was conducted by applying binary logistic regression models for morbidity and 30-day mortality and a negative binomial regression model for hospital stay. All listed ERAS items were considered for univariable tests and variables with P value <0.1 in univariable analysis were included in multivariable analysis. The data are displayed as odds ratios (ORs) with 95% confidence intervals (CIs). Results of the negative binomial regression analysis are presented using the incidence rate ratio. The statistical analysis was conducted with IBM SPSS Statistics version 29 (Armonk, NY: IBM Corp.). A $P < 0.05$ was considered to indicate statistical significance.

RESULTS

Patient Characteristics and Perioperative Course

A total of 615 patients participated in the pancreatic ERAS program at the University Hospital Hamburg-Eppendorf between February 2016 and June 2023. Twenty-one patients were excluded from the analysis because no pancreatic resection was conducted due to inoperable pancreatic carcinoma (Supplemental Figure 1, see http://links.lww.com/AOSO/A414). The demographic and surgical characteristics of the included patients are listed and subgrouped according to 3 study intervals (Table 1).

The inclusion rate of pancreatic patients per month in the ERAS program increased over time, with approximately 80 patients included per year (2016–2018: 5/mo, 2019–2020: 7/m, 2021–2023: 8/mo). The average inclusion rate of pancreatic patients in the ERAS program (EIAS registered) was 78%. The median age of the study population was 65 (IQR: 56–74) years, and most patients (n = 363, 61.1%) were classified as American Society of Anesthesiologists III.

Pancreatic head resection was conducted in 266 patients (44.7%), whereas DP and TP were performed in 87 (14.6%) and 106 (17.8%) patients, respectively. Other pancreatic resections included DPPHR, segment resection, and enucleation (n = 135, 22.7%). Multivisceral and vascular resections were performed in 159 (26.8%) and 206 (34.7%) patients, correspondingly. An open approach was used in 491 patients (82.7%), and most of the laparoscopic procedures (n = 52, 8.8%) were used for DP. From 2021 to 2023, robotic resections have been increasingly established (51 patients total, 35 patients between 2021 and 2023). Malignancy remained the most frequent indication for pancreatic resection (n = 359, 60.5%).

Enhanced Recovery After Surgery Compliance

In the preoperative phase, most items could routinely be addressed with high compliance, including preadmission counseling (n = 579, 98.6%), refrainment from bowel preparation (n = 590, 99.3%), and carbohydrate loading (4n = 50, 81.8%), as well as postoperative nausea and vomiting (n = 563, 96.1%) and antibiotic prophylaxis (n = 585, 98.5%) (Table 2). Intraoperative compliance focused on fluid administration (median: 4780 mL, IQR: 3030–6530 mL), normothermia at the end of surgery (n = 505, 86.6%), and epidural analgesia (n = 477, 80.6%). Postoperatively, thrombosis prophylaxis (n = 591, 99.8%) and stimulation of bowel movement (n = 577, 98.0%) were administered with high compliance. In contrast, postoperative mobilization goals were achieved in only 33.5% (POD1,

TABLE 1.

Patient and Operative Characteristics

	All Patients (N = 594)	2016–2018 (n = 182)	2019–2020 (n = 170)	2021–2023 (n = 242)	P*
Median age in years, median (IQR)	65.0 (56.0–74.0)	67.0 (57.5–76.5)	63.5 (55.5–71.5)	63.0 (54.5–71.5)	**0.022**
Gender, male:female	328:266	99:83	96:74	133:109	0.921
BMI, kg/m^2, mean ± SD	24.6 ± 4.7	24.3 ± 3.9	25.0 ± 4.9	24.7 ± 5.1	0.403
Missing values	3	1		2	
ASA > 2	363 (61.1%)	117 (64.3%)	102 (60.4%)	144 (59.5%)	0.585
Missing values	1		1		
Smoking, n (%)	144 (24.2%)	36 (21.4%)	41 (24.1%)	67 (28.4%)	0.062
Missing values	20	14		6	
Diabetes, n (%)	136 (22.9%)	45 (25.7%)	39 (22.9%)	52 (21.6%)	0.612
Missing values	8	7		1	
Alcohol abuse, n (%)	84 (14.1%)	40 (24.0%)	17 (10.1%)	27 (11.5%)	**<0.001**
Missing values	25	15	2	8	
WHO performance score >2, n (%)	46 (7.7%)	15 (8.2%)	8 (4.7%)	23 (9.5%)	0.197
Missing values	1		1		
Immunosuppression, n (%)	11 (1.9%)	6 (3.4%)	4 (2.4%)	1 (0.4%)	0.075
Missing values	3	3			
Neoadjuvant chemotherapy, n (%)	54 (9.1%)	15 (8.3%)	14 (8.2%)	25 (10.3%)	0.690
Missing values	1	1			
Neoadjuvant radiotherapy, n (%)	11 (1.9%)	9 (5.0%)	0 (0.0%)	2 (0.8%)	**<0.001**
Missing values	1	1			
Previous abdominal surgery, n (%)	256 (43.1%)	70 (38.5%)	93 (54.7%)	93 (38.4%)	**<0.001**
Operation					**<0.001**
prPD, n (%)	147 (24.7%)	66 (36.3%)	46 (27.1%)	35 (14.5%)	
ppPD, n (%)	119 (20.0%)	28 (15.4%)	28 (16.5%)	63 (26.0%)	
DP, n (%)	87 (14.6%)	13 (7.1%)	27 (15.9%)	47 (19.4%)	
TP, n (%)	106 (17.8%)	41 (22.5%)	34 (20.0%)	31 (12.8%)	
Other, n (%)	135 (22.7%)	34 (18.7%)	35 (20.6%)	66 (27.3%)	
Multivisceral resection, n (%)	159 (26.8%)	52 (28.6%)	44 (25.9%)	57 (23.6%)	0.504
Colonic/rectal resection	40	6	13	21	
(Atypical) Liver resection	63	28	14	21	
Other	56	18	17	15	
Technique					**<0.001**
Open, n (%)	491 (82.7%)	152 (83.5%)	148 (87.1%)	191 (78.9%)	
Laparoscopic, n (%)	52 (8.8%)	23 (12.6%)	13 (7.6%)	16 (6.6%)	
Robotic, n (%)	51 (8.6%)	7 (3.8%)	16 (6.6%)	35 (14.5%)	
Elective, n (%)	566 (95.3%)	178 (97.8%)	167 (98.2%)	221 (91.3%)	**0.005**
Operating time in minute, mean ± SD	340.5 ± 114.2	332.9 ± 111.5	336.0 ± 107.0	349.6 ± 120.8	0.274
Missing values	3	—	—	3	
Pancreatic texture (soft), n (%)	171 (46.1%)	60 (50.0%)	35 (37.6%)	76 (48.1%)	0.159
Missing values	223	62	107	84	
Prophylactic drainage, n (%)	590 (99.7%)	178 (98.9%)	170 (100.0%)	242 (100.0%)	0.101
Missing values	2	2			
Malignancy, n (%)	359 (60.5%)	132 (72.5%)	97 (57.4%)	130 (53.7%)	**<0.001**

Bold values indicate $P \leq 0.05$.

*Categorical variables: χ^2 test, continuous variables: 1-way ANOVA.

ANOVA indicates analysis of variance; ASA, American Society of Anesthesiologists; BMI, body mass index; ppPD, pylorus-preserving pancreaticoduodenectomy; prPD, pylorus-resection pancreaticoduodenectomy; WHO, World Health Organization.

>2 hours), 3.6% (POD2, >6 hours), and 11.6% (POD3, >6 hours), respectively. Early removal of urinary catheters was fulfilled in 36.2% of the patients. The latter item, however, was significantly improved during the last study interval. The average total compliance reached 61.2% and was lowest in the postoperative phase (36.0%). Generally, a moderate increase in mean total compliance rates was observed during recent years (2016–2019: 60.5%; 2019–2020: 59.8; 2021–2023: 62.8%) (Table 2).

The Effect of Enhanced Recovery After Surgery Compliance on Postoperative Outcomes

Severe complications (CDC ≥ 3a) occurred in 236 patients (39.7%) (Table 3). Any pulmonary complications (including all CDC grades) were most common (n = 124, 22.3%), followed by clinically relevant POPF and DGE (n = 126 [21.2%] and n = 87 [14.7%], respectively). The median hospital stay was 13 days (IQR: 7.5–18.5 days).

We next sought to determine whether high ERAS compliance was associated with an alteration in postoperative outcomes of the entire study cohort. High (≥70%) compliance was achieved in 90 patients (15.2%) (Supplemental Table 3, see http://links.lww.com/AOSO/A414). This subgroup was characterized by significantly younger patients, a higher proportion of DP (33.3% vs 11.3%, $P < 0.001$), and a shorter operating time (274 vs 352 minutes, $P < 0.001$). In line with this, a minimally-invasive approach was performed more frequently (31.1% vs 14.8%, $P < 0.001$) and more operations were performed for benign lesions (64.4% vs 38.9%, $P < 0.001$). This resulted in a reduced rate of major morbidity (CDC ≥ 3a), except for POPF, (18.9% vs. 43.5%, $P < 0.001$) and a shorter duration of hospital (median 9.0 vs 14.0 days, $P < 0.001$). (Supplemental Table 4, see http://links.lww.com/AOSO/A414).

Uni- and multivariable analyses were performed including the entire cohort to identify single ERAS items that were associated with the clinically relevant outcome parameters morbidity,

TABLE 2.

Perioperative Compliance

	All Patients (N = 594)	2016–2018 (n = 182)	2019–2020 (n = 170)	2021–2023 (n = 242)	P*
Preadmission counseling	579 (98.6%)	178 (98.9%)	162 (98.2%)	239 (98.8%)	0.832
Carbohydrate loading	450 (81.8%)	165 (93.2%)	108 (78.3%)	177 (75.3%)	**<0.001**
No bowel preparation	590 (99.3%)	1 (0.6%)	0.0 (0.0%)	0.0 (0.0%)	0.316
Antibiotic prophylaxis	585 (98.5%)	179 (98.4%)	167 (98.2%)	239 (98.8%)	0.898
PONV prophylaxis	563 (96.1%)	158 (90.3%)	167 (98.2%)	238 (98.8%)	**<0.001**
Normothermia	505 (86.6%)	162 (90.0%)	132 (80.5%)	211 (88.3%)	**0.022**
Intraoperative intravenous in mL, mean ± SD	5972.3 ± 3793.4	5046.1 ± 2497.6	5640.1 ± 3258.4	6335.3 ± 4200.4	**<0.001**
Epidural analgesia	477 (80.6%)	161 (88.5%)	135 (79.4%)	181 (75.4%)	**0.003**
Mobilization					
OP day	179 (30.4%)	94 (51.9%)	21 (12.4%)	64 (26.9%)	**<0.001**
POD1 > 2 h	190 (33.5%)	87 (49.2%)	35 (21.3%)	68 (30.1%)	**<0.001**
POD2 > 6 h	20 (3.6%)	4 (2.3%)	9 (5.6%)	7 (3.1%)	0.227
POD3 > 6 h	65 (11.6%)	7 (4.1%)	18 (11.0%)	40 (17.9%)	**<0.001**
Thrombosis prophylaxis	591 (99.8%)	182 (100.0%)	167 (99.4%)	242 (100.0%)	0.283
Gut stimulation	577 (98.0%)	166 (93.3%)	170 (100.0%)	241 (100.0%)	**<0.001**
Early removal of urinary catheter	189 (36.2)	40 (28.4%)	44 (27.7%)	105 (47.3%)	**<0.001**
Mean total compliance ± SD	61.2% ± 9.1%	60.5% ± 10.2%	59.8% ± 9.5%	62.8% ± 7.7%	**0.002**
Mean preadmission compliance ± SD	81.6% ± 23.7%	75.6% ± 27.7%	80.2% ± 25.5%	87.0% ± 17.0%	**<0.001**
Mean preoperative compliance ± SD	81.1% ± 12.2%	90.5% ± 13.1%	76.2% ± 9.9%	77.4% ± 8.4%	**<0.001**
Mean intraoperative compliance ± SD	86.3% ± 16.3%	81.5% ± 18.2%	87.3% ± 14.4%	89.1% ± 15.3%	**<0.001**
Mean postoperative compliance ± SD	36.0% ± 14.7%	34.0% ± 13.8%	34.9% ± 15.6%	38.3% ± 14.4%	**0.005**

Bold values indicate $P \leq 0.05$.

*Categorical variables: χ^2 test, continuous variables: 1-way ANOVA.

ANOVA indicates analysis of variance; PONV, postoperative nausea and vomiting.

TABLE 3.

Postoperative Course and Morbidity

Complications	Patient Cohort (n = 594)
Morbidity (CDC ≥ 3a)	236 (39.7%)
Pulmonary complications	124 (22.3%)
Missing values	38
POPF	
Biochemical leakage	46 (7.7%)
Grade B	91 (15.3%)
Grade C	35 (5.9%)
DGE	87 (14.7)
Missing values	2
Biliary fistula	42 (7.1%)
PPH	47 (7.9%)
Urinary tract infection	26 (4.4%)
Missing values	1
Sepsis	52 (8.8%)
Cardiovascular complications	81 (13.6%)
Renal, hepatic, or gastrointestinal complications	139 (23.4%)
Median hospital stay, d (IQR)	13.0 (7.5–18.5)
Primary stay in ICU, median days (IQR)	0 (0–2)

ICU indicates intensive care unit.

mortality, and hospital stay (Table 4 and Supplemental Tables 5a and 5b, see http://links.lww.com/AOSO/A414). Multivariable predictors were: restrictive intraoperative fluid management (P = 0.008), mobilization on POD1 (P = 0.003), and early removal of urinary catheters for the outcome "morbidity" (P = 0.025); mobilization on POD1 (P = 0.018) and gut stimulation (P = 0.024) for "mortality"; and mobilization on POD1 (P = 0.033) and early removal of urinary catheters (P = 0.008) for a shorter duration of hospital stay.

However, to avoid a potential bias by the less complex and minimally-invasive operations, the association of single ERAS items with outcome variables was separately assessed after PD (n = 266, including vascular resections in 30%) and non-PD operations (n = 328), respectively (Table 5 and Supplemental Tables 6 and 7, see http://links.lww.com/AOSO/A414). High overall compliance (≥70%) was found in only 7.9% (21 of 266 patients) with PD and 21.0% (69 of 328 patients) in non-PD patients. High compliance was further associated with reduced rates of major postoperative complications (CDC ≥ 3a, P < 0.001) and a significantly shorter median hospital stay (9 days, IQR: 6.0–9.0 days vs 13 days, IQR: 8.0–18.0; P < 0.001) in non-PD operations, only. Less complications in the latter subcohort were associated with early mobilization on POD1 (OR: 0.514; CI: 0.267–0.991; P = 0.047) and a restrictive intraoperative fluid management (OR: 0.453; CI: 0.257–0.799; P = 0.006). In addition, early mobilization was further associated with a shorter hospital stay duration (incidence rate ratio: 0.709; CI: 0.531–0.948; P = 0.020).

In the subcohort of PD cases, the median duration of hospital stay was 12 days (IQR: 6.5–17.5) versus 15 days (IQR: 10.0–20.0) in patients with ≥70% and <70% compliance (P = 0.100), respectively. Compared with non-PD cases, early mobilization was the only ERAS item with a significant effect on outcome and was associated with a reduced morbidity (OR: 0.414; CI: 0.221–0.776; P = 0.006; Table 5). The compliance of early mobilization on POD1 was similar after PD operations without (n = 155, 29.7%) and with (n = 106, 31.4%) vascular resections (P = 0.781). However, the mobilization per protocol on the day of operation was less frequently achieved if a simultaneous vascular resection was performed: 19.0% versus 30.3% in cases without vascular resection (P = 0.043).

DISCUSSION

The present study reports on a large cohort of patients who were treated within a pancreatic ERAS program at a certified ERAS center of excellence. The ERAS program was continuously staffed with ERAS nurses, and data were recorded using the EIAS. An important feature of the study is the application of ERAS recommendations for PD to all pancreatic resections, including total, distal, and segmental pancreatectomies; enucleations; and DPPHRs as well as simultaneous vascular resections. Currently, minimally-invasive (laparoscopic and robotic) approaches are the standard for distal pancreatectomies, DPPHR, and localized pancreatic head tumors at the authors' institution. This finding is in line with randomized

TABLE 4.

Association of ERAS Protocol Compliance and Single Items With Morbidity, Mortality, and Duration of Hospital Stay (Multivariable Analysis) in the Entire Study Cohort (594 Patients)

	Odds Ratio*	95% CI		*P*
Morbidity (CDC ≥ 3a)				
Restrictive intraoperative intravenous fluid administration (<median)	0.592	0.403	0.871	**0.008**
Mobilization 2 h on POD1	0.515	0.331	0.801	**0.003**
Minimally-invasive surgery	0.746	0.433	1.284	0.290
Early removal of urinary catheter	0.610	0.395	0.941	**0.025**
30-day mortality				
Restrictive intraoperative intravenous fluid administration (<median)	0.687	0.352	1.340	0.271
Mobilization 2 h on POD1	0.355	0.151	0.835	**0.018**
Minimally-invasive surgery	0.779	0.291	2.089	0.620
Gut stimulation	0.189	0.045	.802	**0.024**
Hospital stay*				
Carbohydrate loading	1.056	0.817	1.365	0.676
Minimally-invasive surgery	0.835	0.647	1.076	0.164
Restrictive intraoperative intravenous fluid administration (<median)	0.851	0.647	1.076	0.115
Mobilization 2 h on POD1	0.793	0.640	0.982	**0.033**
Early removal of urinary catheter	0.751	0.607	0.929	**0.008**

Bold values indicate $P \leq 0.05$.

*For hospital stay analysis, the incidence rate ratio (IRR) was calculated instead of the odds ratio.

TABLE 5.

Association of ERAS Protocol Compliance and Single Items With Morbidity, Mortality, and Duration of Hospital Stay (Multivariable Analysis) Stratified by Pancreaticoduodenectomy (PD) and Nonpancreaticoduodenectomy (non-PD)

Outcome Stratified by Type of Operation	Odds Ratio*	95% CI		*P*
PD (n = 266)				
Morbidity (CDC ≥ 3a)				
Epidural analgesia	0.470	0.220	1.005	0.051
Mobilization 2 h on POD1	0.414	0.221	0.776	**0.006**
Early removal of urinary catheter	0.717	0.383	0.383	0.301
Hospital stay*				
Carbohydrate loading	0.813	0.523	1.263	0.357
Mobilization 2 h on POD1	0.925	0.670	1.278	0.638
Early removal of urinary catheter	0.790	0.565	1.103	0.166
Non-PD (n = 328)				
Morbidity (CDC ≥ 3a)				
Restrictive intraoperative intravenous fluid administration (< median)	0.453	0.257	0.799	**0.006**
Mobilization 2 h on POD1	0.514	0.267	0.991	**0.047**
Minimally-invasive surgery	0.553	0.237	1.291	0.171
Early removal of urinary catheter	0.703	0.371	1.331	0.279
30-day mortality				
Restrictive intraoperative intravenous fluid administration (<median)	0.630	0.245	1.620	0.337
Mobilization 2 h on POD1	0.337	0.096	1.189	0.091
Minimally-invasive surgery	0.275	0.035	2.160	0.220
Hospital stay*				
Carbohydrate loading	1.162	0.846	1.597	0.354
Minimally-invasive surgery	0.745	0.532	1.043	0.087
Restrictive intraoperative intravenous fluid administration (<median)	0.807	0.612	1.064	0.129
Mobilization 2 h on POD1	0.709	0.531	0.948	**0.020**
Early removal of urinary catheter	0.785	0.587	1.050	0.102

Bold values indicate $P \leq 0.05$.

*For hospital stay analysis, the incidence rate ratio (IRR) was calculated instead of the odds ratio.

noninferiority trials investigating minimally-invasive pancreatic surgery.[18–20] The data demonstrated that a certified pancreatic ERAS setting involving the implementation of all recommended items can be sustained for a period of 8 years without significant decreases in inclusion or total compliance rates. This is important as a recent systematic review showed that the median number of implemented items in ERAS centers is only 16, and compliance is reported in only one-third of the centers.[3]

The compliance rates observed in the reported pre-, intra-, and postoperative periods were even slightly superior to the multi-institutional results in an earlier phase after ERAS implementation.[6] Although not all patients admitted for pancreatic resection were treated according to the full ERAS program, a greater proportion (up to 70%) was included in the last study interval. Patients were considered for the ERAS program without prior selection; however, preadmission counseling was a prerequisite (>98%) for entering the program. Some patients failed to receive counseling due to the urgent need for surgery, lack of human resources, or logistic failure.

Although the total compliance of all patients reached >61%, the postoperative compliance of some patients greatly varied, which is similar to recent reports.[6] The main reason for low postoperative compliance is the failure to achieve postoperative mobilization goals within 2–6 hours during the first 3 days.

There is an ongoing debate on the effect of mobilization programs not only in pancreatic surgery. For example, randomized data indicated that mobilization on the day of pancreatic surgery can ameliorate early oxygenation.[21] However, no specific mobilization protocol can be recommended to further reduce morbidity or hospital stay duration in an ERAS setting.[22] Consequently, the updated ERAS guideline recommends starting early active mobilization beginning on the day of surgery without defining hourly targets (EIAS version 5.7.9 released on October 16).[5] As a result, the postoperative compliance rate will likely increase in many centers.

Early mobilization of the patients after pancreatic resection nonetheless remains a key challenge of ERAS research. The present study undoubtedly underlines the importance of early mobilization during the first postoperative day as a persistent and strong outcome predictor and prompts us to investigate whether mobilization has an innate effect on the recovery process or whether low mobilization activity is a mere side effect of a preexisting impaired health status after major operations and the development of complications. Prospective activity tracking with objective target goals (eg, step counts) and further evaluation of specific mobilization protocols are required to build up stronger evidence in this field.[22] Notably, no preoperative ERAS item significantly affected short-term outcomes, and these items should be tested and verified in further trials. Prehabilitation programs are promising adjuncts to the concept used in other gastrointestinal fields and are now covered by the updated guidelines.[5,23,24]

In addition to early mobilization, restrictive fluid management and early removal of urinary catheters were key determinants of improved short-term outcomes in the present study. The timely removal of urinary catheters is sometimes impeded by urinary retention or the lack of ambulation.[25] Additionally, critically ill patients frequently need intensified monitoring of urinary clearance and fluid balance requiring urinary catheterization. The present study indicates a positive correlation between early removal of urinary catheters and lower morbidity, but cannot ultimately solve the question of whether the early removal causatively leads to less complications. It seems more likely that more complex and longer operations frequently necessitated prolonged catheterization. Epidural analgesia can also delay the removal of urinary catheters and alternative options include transversus abdominis plane blocks, which are also considered by the current ERAS guidelines.[5] The present data showed that there was even a trend toward less complications in the patient subgroup with PD under epidural analgesia, but clinical consequences cannot be deduced from this statistical observation.

This study has several limitations that should be considered when attempting to draw further conclusions. Although the data were prospectively recorded in a registry database, the results were retrospective, and causal associations between different items and outcome variables (eg, mobilization and morbidity) could not be determined. Furthermore, preoperative counseling and consent were prerequisites for inclusion in the database. As a peculiar characteristic, the study reported the compliance and outcome results for all pancreatic resections, and PD operations were the focus of subgroup analysis only. However the inclusion of other pancreatic operations in the ERAS program may be warranted because the presented results underscore the beneficial application of ERAS for non-PD cases and are an additional pertinent finding.

In conclusion, the present study demonstrated that a certified full pancreatic ERAS setting can be stably sustained over several years, applied for all pancreatic resections, and improved even further. A mandatory prerequisite is a dedicated interdisciplinary team that includes trained ERAS nurses. Patients with a high ERAS compliance ≥70% constitute a highly selected subgroup with low morbidity and mortality and a shorter duration of hospital stay. However, only a minority (<10%) of patients after PD achieve this high compliance level. Future emphasis should be placed on the key items early mobilization of POD1, restrictive fluid management, early drain/urinary catheter removal, and minimally-invasive surgery, which are associated with improved outcomes, as well as on prehabilitation, to foster further progress in the pancreatic ERAS concept and to increase the number of patients with high compliance.

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